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Wells et al

Application Number

09/385404

Filed

2/7/95

Paper No. *36*

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United States Patent [19]

Weiss et al.

[11] Patent Number: 5,750,376

[45] Date of Patent: May 12, 1998

[54] IN VITRO GROWTH AND PROLIFERATION
OF GENETICALLY MODIFIED
MULTIPOTENT NEURAL STEM CELLS AND
THEIR PROGENY

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abandoned, Ser. No. 385,404, Feb. 7, 1995, abandoned, Ser.
No. 359,945, Dec. 20, 1994, abandoned, Ser. No. 376,062,
Jan. 20, 1995, abandoned, Ser. No. 149,508, Nov. 9, 1993,
abandoned, Ser. No. 311,099, Sep. 23, 1994, abandoned, and
Ser. No. 338,730, Nov. 14, 1994, abandoned, which is a
continuation-in-part of Ser. No. 726,812, Jul. 8, 1991, aban-
doned, said Ser. No. 385,404, Feb. 7, 1995, abandoned, is a
continuation of Ser. No. 961,813, Oct. 16, 1992, abandoned,
which is a continuation-in-part of Ser. No. 726,812, Jul. 8,
1991, abandoned, said Ser. No. 359,345, Dec. 20, 1994,
abandoned, is a continuation of Ser. No. 221,655, Apr. 1,
1994, abandoned, which is a continuation of Ser. No.
967,622, Oct. 28, 1992, abandoned, which is a continuation-
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of Ser. No. 10,829, Jan. 29, 1993, abandoned, which is
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abandoned, said Ser. No. 270,412, Jul. 5, 1994, abandoned,
Ser. No. 149,508, Nov. 9, 1993, abandoned, and Ser. No.
311,099, Sep. 23, 1994, abandoned, each is a continuation-
in-part of Ser. No. 726,812, Jul. 8, 1991, abandoned.

[51] Int. Cl.⁶ C12N 5/00; C12N 5/08;
C12N 5/10; C12P 1/00

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435/325; 435/368; 435/377; 435/384; 435/392;
435/395

[58] Field of Search 435/240.2, 172.3,
435/69.1, 69.52, 325, 368, 377, 384, 392,
395

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ABSTRACT

A method for producing genetically modified neural cells
comprises culturing cells derived from embryonic, juvenile,
or adult mammalian neural tissue with one or more growth
factors that induce multipotent neural stem cells to proliferate
and produce multipotent neural stem cell progeny
which include more daughter multipotent neural stem cells
and undifferentiated progeny that are capable of differentiating
into neurons, astrocytes, and oligodendrocytes. The
proliferating neural cells can be transfected with exogenous
DNA to produce genetically modified neural stem cell
progeny. The genetic modification can be for the production
of biologically useful proteins such as growth factor
products, growth factor receptors, neurotransmitters, neu-
rotransmitter receptors, neuropeptides and neurotransmitter
synthesizing genes. The multipotent neural stem cell progeny
can be continuously passaged and proliferation reinitiated
in the presence of growth factors to result in an
unlimited supply of neural cells for transplantation and other
purposes. Culture conditions can be provided that induce the
genetically modified multipotent neural stem cell progeny to
differentiate into neurons, astrocytes, and oligodendrocytes
in vitro.

40 Claims, 3 Drawing Sheets